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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/591,743	08/13/2008	Stephen C. Alley	018891-000720US	6300

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EXAMINER	
HUYNH, PHUONG N	

ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
08/14/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/591,743	ALLEY ET AL.	
	Examiner	Art Unit	
	PHUONG HUYNH	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *One* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10,11,13,34-39,43,45-47,50-54,58,62-65 and 73-112* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *10-11, 13, 34-39, 43, 45-47, 50-54, 58, 62-65, and 73-112* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 10-11, 13, 34-39, 43, 45-47, 50-54, 58, 62-65, and 73-112 are pending.

REQUIREMENT FOR UNITY OF INVENTION

As provided in 37 CFR 1.475(a), a national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept ("requirement of unity of invention"). Where a group of inventions is claimed in a national stage application, the requirement of unity of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

The determination whether a group of inventions is so linked as to form a single general inventive concept shall be made without regard to whether the inventions are claimed in separate claims or as alternatives within a single claim. See 37 CFR 1.475(e).

When Claims Are Directed to Multiple Categories of Inventions:

As provided in 37 CFR 1.475(b), a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories:

(1)A product and a process specially adapted for the manufacture of said product; or

(2)A product and process of use of said product; or

(3)A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or

(4)A process and an apparatus or means specifically designed for carrying out the said process; or

(5)A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process.

Otherwise, unity of invention might not be present. See 37 CFR 1.475(c).

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

I. Claims 10-11, 13, 77 and 79-106, drawn to an **antibody**, comprising points of conjugation for a cytotoxic or cytostatic agent, wherein at least one point of conjugation for the cytotoxic or cytostatic agent on the antibody can be readily assigned, and wherein less than all possible points of conjugation are available for conjugation to the cytotoxic or cytostatic agent.

II. Claims 34-39, 43, 45-47, 50-54, 58, 62-65 and 73-75, drawn to a **method of reducing and conjugating a drug to an antibody**.

III. Claims 73-74, drawn to a **method for a conjugate of a protein other than antibody** having one or more disulfide bonds and a drug.

IV. Claims 77, 84, 86 and 93, drawn to a partially loaded, modified protein, the modified protein is a specific **receptor**.

V. Claims 77, 84, 86 and 93, drawn to a partially loaded, modified protein, the modified protein is a specific **receptor ligand**.

VI. Claims 77, 84, 86 and 93, drawn to a partially loaded, modified protein, the modified protein is a specific **hormone**.

VII. Claims 77, 84, 86 and 93, drawn to a partially loaded, modified protein, the modified protein is a specific **cytokine**.

VIII. Claims 107-112, drawn to a method for the treatment of **cancer** in a patient, comprising administering to the patient an amount of a specific modified antibody.

IX. Claims 107-112, drawn to a method for the treatment of **a specific immune disease other than autoimmune disease** in a patient, comprising administering to the patient an amount of a specific modified antibody.

\X. Claims 107-112, drawn to a method for the treatment of **a specific autoimmune disease** in a patient, comprising administering to the patient an amount of a specific modified antibody.

XI. Claims 107-112, drawn to a method for the treatment of **a specific infectious disease** in a patient, comprising administering to the patient an amount of a specific modified antibody.

Linking claims 76 and 78 will be examined along with Groups I, IV, V, VI, and VII if any one of said Groups is elected.

Claims 76 and 78 link inventions I, IV, V, VI, or VII. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim, claims 76 and 78. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

The Groups of inventions listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Groups I-XI lack unity of invention because the groups do not share same or corresponding technical feature.

Group I lacks unity of invention because even though the invention requires the technical feature of an antibody comprising one or more points of conjugation for cytotoxic agent or cytostatic agent on the antibody and less than all possible points of conjugation are available for conjugation to the cytotoxic or cytostatic agent, this technical feature is not a special technical feature as it does not make a contribution over the prior art in view of Francisco et al (Blood 102(4): 1458-1465, August 2003, PTO 1449) as evidenced by Saito et al (Advanced Drug Delivery Reviews 55: 199-215, 2003; PTO 1449).

Francisco et al teach a partially reduced antibody such as anti-CD30 comprising at least one points of conjugation for a cytotoxic agent such as monomethylvaline (MMAE) (see entire document, page 1459, col. 2, conjugate preparation, in particular). The reference teaches approximately 8 drugs can be conjugated per antibody molecule (see page 1460, col. 1, caption of Figure 1, in particular). The

reference “approximately" and “partial reduction” imply that not all points on the antibody were conjugated. Further, the term "comprising” is open-ended. It expands the claimed antibody to include additional molecule such as linker peptide of the reference.

Evidentiary reference Saito et al teach site-directed conjugation using endogenous sulfhydryls of antibody to various cytotoxic agents such as doxorubicin (Dox)-antibody conjugate (see page 206, col. 1, para. 3.2., in particular). Saito et al teach selectively reducing interchain disulfide bonds in the antibody, a total of four S-S bonds (a total of eight points of conjugation), in the hinge region and between the light and heavy chains, which can be conjugated to equivalently of eight drug molecules per antibody, see page 206, col. 1, in particular. Even if cysteine is not readily available for conjugation, it can be incorporated into recombinantly expressed proteins by site-directed amino acid substitution. Thus it is within the purview of one of ordinary skill in the art to site specific conjugating any cytotoxic agent to any antibody or protein by partially reduction antibody or protein for conjugation as taught by Francisco as evidenced by Saito et al.

Because Applicant’s inventions do not contribute a special technical feature when viewed over the prior art, the inventions lack unity of invention.

Accordingly, Groups I-XI are not so linked as to form a single general inventive concept and restriction is proper.

Claim 107 is generic to the following disclosed patentably distinct species: autoimmune disease identifiable at paragraph [0160], or infectious disease identifiable at page [0164]. The species are independent or distinct because as disclosed the different species have mutually exclusive characteristics for each identified species. In addition, these species are not obvious variants of each other based on the current record. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

Applicant is further required under **35 U.S.C. 121 and 372** to elect a single disclosed species of autoimmune disease or infectious disease if Group X or XI is elected for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

There is an examination and search burden for these patentably distinct species due to their mutually exclusive characteristics. The species require a different field of search (e.g., searching different classes/subclasses or electronic resources, or employing different search queries); and/or the prior art applicable to one species would not likely be applicable to another species; and/or the species are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species to be examined even though the requirement may be traversed (37 CFR 1.143) **and (ii) identification of the claims encompassing the elected species**, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

The election of the species may be made with or without traverse. To preserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the election of species requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected species.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the species unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other species.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in

scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently filed petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 C.F.R. § 1.17(h).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh, Ph.D. whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Thursday from 9:00 a.m. to 6:30 p.m. and alternate Friday from 9: 00 a.m. to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen B O'Hara can be reached on (571) 272-0878. The IFW official Fax number is (571) 273-8300.

Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Phuong Huynh/
Primary Examiner, Art Unit 1644
August 14, 2009